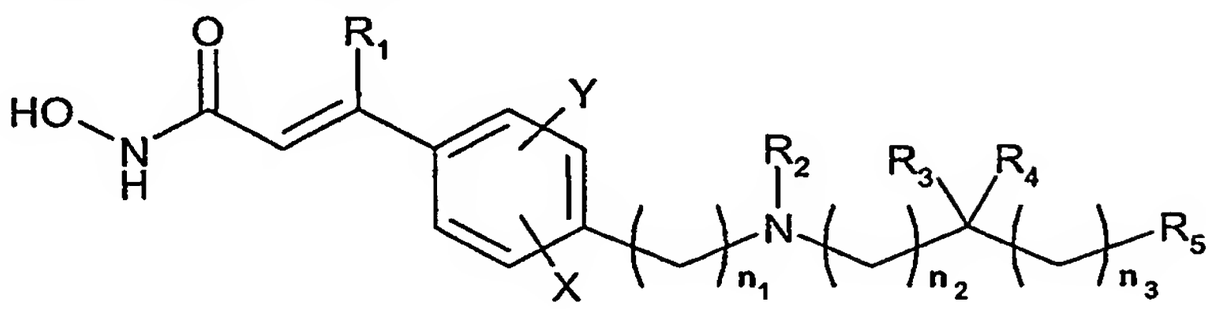
What is claimed is:

1. A combination comprising

(a) death receptor ligand, and

(b) a histone deacetylase inhibitor of formula (I)



(I)

wherein

R_1 is H; halo; or a straight-chain C_1-C_6alkyl, especially methyl, ethyl or *n*-propyl, which methyl, ethyl and *n*-propyl substituents are unsubstituted or substituted by one or more substituents described below for alkyl substituents;

R_2 is selected from H; C_1-C_{10}alkyl, preferably C_1-C_6alkyl, e.g., methyl, ethyl or -CH_2CH_2-OH; C_4-C_9cycloalkyl; C_4-C_9heterocycloalkyl; C_4-C_9heterocycloalkylalkyl; cycloalkylalkyl, e.g., cyclopropylmethyl; aryl; heteroaryl; arylalkyl, e.g., benzyl; heteroarylalkyl, e.g., pyridylmethyl; -$(CH_2)_nC(O)R_6$; -$(CH_2)_nOC(O)R_6$; amino acyl; HON-C(O)-CH=C(R_1)-aryl-alkyl-; and -$(CH_2)_nR_7$;

R_3 and R_4 are the same or different and, independently, H; C_1-C_6alkyl; acyl; or acylamino; or

R_3 and R_4, together with the carbon to which they are bound, represent C=O, C=S or C=NR_8; or

R_2, together with the nitrogen to which it is bound, and R_3, together with the carbon to which it is bound, can form a C_4-C_9heterocycloalkyl; a heteroaryl; a polyheteroaryl; a non-aromatic polyheterocycle; or a mixed aryl and non-aryl polyheterocycle ring;

R_5 is selected from H; C_1-C_6alkyl; C_4-C_9cycloalkyl; C_4-C_9heterocycloalkyl; acyl; aryl; heteroaryl; arylalkyl, e.g., benzyl; heteroarylalkyl, e.g., pyridylmethyl; aromatic polycycles; non-aromatic polycycles; mixed aryl and non-aryl polycycles; polyheteroaryl; non-aromatic polyheterocycles; and mixed aryl and non-aryl polyheterocycles;

n, n_1, n_2 and n_3 are the same or different and independently selected from 0-6, when n_1 is 1-6, each carbon atom can be optionally and independently substituted with R_3 and/or R_4;

X and Y are the same or different and independently selected from H; halo; C_1-C_4alkyl, such as CH_3 and CF_3; NO_2; $C(O)R_1$; OR_9; SR_9; CN; and $NR_{10}R_{11}$;

R_6 is selected from H; C_1-C_6alkyl; C_4-C_9cycloalkyl; C_4-C_9heterocycloalkyl; cycloalkylalkyl, e.g., cyclopropylmethyl; aryl; heteroaryl; arylalkyl, e.g., benzyl and 2-phenylethenyl; heteroarylalkyl, e.g., pyridylmethyl; OR_{12}; and $NR_{13}R_{14}$;

R_7 is selected from OR_{15}; SR_{15}; $S(O)R_{16}$; SO_2R_{17}; $NR_{13}R_{14}$; and $NR_{12}SO_2R_6$;

R_8 is selected from H; OR_{15}; $NR_{13}R_{14}$; C_1-C_6alkyl; C_4-C_9cycloalkyl; C_4-C_9heterocycloalkyl; aryl; heteroaryl; arylalkyl, e.g., benzyl; and heteroarylalkyl, e.g., pyridylmethyl;

R_9 is selected from C_1-C_4alkyl, e.g., CH_3 and CF_3; C(O)-alkyl, e.g., $C(O)CH_3$; and $C(O)CF_3$;

R_{10} and R_{11} are the same or different and independently selected from H; C_1-C_4alkyl; and -C(O)-alkyl;

R_{12} is selected from H; C_1-C_6alkyl; C_4-C_9cycloalkyl; C_4-C_9heterocycloalkyl; C_4-C_9heterocycloalkylalkyl; aryl; mixed aryl and non-aryl polycycle; heteroaryl; arylalkyl, e.g., benzyl; and heteroarylalkyl, e.g., pyridylmethyl;

R_{13} and R_{14} are the same or different and independently selected from H; C_1-C_6alkyl; C_4-C_9cycloalkyl; C_4-C_9heterocycloalkyl; aryl; heteroaryl; arylalkyl, e.g., benzyl; heteroarylalkyl, e.g., pyridylmethyl; amino acyl; or

R_{13} and R_{14}, together with the nitrogen to which they are bound, are C_4-C_9heterocycloalkyl; heteroaryl; polyheteroaryl; non-aromatic polyheterocycle; or mixed aryl and non-aryl polyheterocycle;

R_{15} is selected from H; C_1-C_6alkyl; C_4-C_9cycloalkyl; C_4-C_9heterocycloalkyl; aryl; heteroaryl; arylalkyl; heteroarylalkyl; and $(CH_2)_mZR_{12}$;

R_{16} is selected from C_1-C_6alkyl; C_4-C_9cycloalkyl; C_4-C_9heterocycloalkyl; aryl; heteroaryl; polyheteroaryl; arylalkyl; heteroarylalkyl; and $(CH_2)_mZR_{12}$;

R_{17} is selected from C_1-C_6alkyl; C_4-C_9cycloalkyl; C_4-C_9heterocycloalkyl; aryl; aromatic polycycles; heteroaryl; arylalkyl; heteroarylalkyl; polyheteroaryl and $NR_{13}R_{14}$;

m is an integer selected from 0-6; and

Z is selected from O; NR_{13}; S; and S(O),

or a pharmaceutically acceptable salt thereof.

2. A method for the prevention or treatment of proliferative diseases, in a mammal, which comprises treating the mammal with pharmaceutically effective amounts of a combination of:

(a) death receptor ligand, and

(b) a histone deacetylase inhibitor of formula (I) according to claim 1.

3. The combination according to Claim 1, wherein the death receptor ligand is TRAIL, TRAIL/Apo-2L, TRAIL mimetics, agonistic antibodies, or other agents that can bind to DR4 and DR5 triggering the activity of caspase-8 and apoptosis through the assembly of a cell-membrane associated multi-protein death inducing signaling complex (DISC).

4. The combination of Claim 1, wherein the HDAI is selected from the group consisting of *N*-hydroxy-3-[4-[[(2-hydroxyethyl)[2-(*1H*-indol-3-yl)ethyl]-amino]methyl]phenyl]-*2E*-2-propenamide, *N*-hydroxy-3-[4-[[[2-(*1H*-indol-3-yl)ethyl]-amino]methyl]phenyl]-*2E*–2-propenamide and *N*-hydroxy-3-[4-[[[2-(2-methyl-*1H*-indol-3-yl)-ethyl]-amino]methyl]phenyl]-*2E*-2-propenamide, or a pharmaceutically acceptable salt thereof.

5. The combination of Claim 1 for the prevention or treatment of leukemia.

6. The method of Claim 2, wherein the mammal is a human.

7. The combination of Claim 1 for the prevention or treatment of acute myeloid leukemia (AML).

8. A combined preparation which comprises:

(a) one or more unit dosage forms of a death receptor ligand; and

(b) one or more unit dosage forms of a HDAI of formula (I) of Claim 1.

9. The combined preparation according to Claim 8, wherein the death receptor ligand is TRAIL, TRAIL/Apo-2L, TRAIL mimetics, agonistic antibodies, or other agents that can bind to DR4 and DR5 triggering the activity of caspase-8 and apoptosis through the assembly of a cell-membrane associated multi-protein DISC.

10. The combined preparation of Claim 9, wherein the histone deacetylase inhibitor is selected from the group consisting of *N*-hydroxy-3-[4-[[(2-hydroxyethyl)[2-(*1H*-indol-3-

yl)ethyl]-amino]methyl]phenyl]-*2E*-2-propenamide, *N*-hydroxy-3-[4-[[[2-(*1H*-indol-3-yl)ethyl]-amino]methyl]phenyl]-*2E*-2-propenamide and *N*-hydroxy-3-[4-[[[2-(2-methyl-*1H*-indol-3-yl)-ethyl]-amino]methyl]phenyl]-*2E*-2-propenamide, or a pharmaceutically acceptable salt thereof.

11. A method of treating or preventing premalignant proliferative diseases in a mammal which comprises treating the mammal with a combination of:

(a) a pharmaceutically effective amount of a death receptor ligand; and

(b) a pharmaceutically effective amount of *N*-hydroxy-3-[4-[[(2-hydroxyethyl)[2-(*1H*-indol-3-yl)ethyl]-amino]methyl]phenyl]-*2E*-2-propenamide, *N*-hydroxy-3-[4-[[[2-(*1H*-indol-3-yl)ethyl]-amino]methyl]phenyl]-*2E*-2-propenamide or *N*-hydroxy-3-[4-[[[2-(2-methyl-*1H*-indol-3-yl)-ethyl]-amino]methyl]phenyl]-*2E*-2-propenamide; or a pharmaceutically effective salt thereof.

12. The method according to Claim 11, wherein the death receptor ligand is TRAIL, TRAIL/Apo-2L, TRAIL mimetics, agonistic antibodies, or other agents that can bind to DR4 and DR5 triggering the activity of caspase-8 and apoptosis through the assembly of a cell-membrane associated multi-protein DISC.

13. A method of treating or preventing proliferative diseases in a mammal which comprises treating the mammal with a combination of:

(a) a pharmaceutically effective amount of a death receptor ligand; and

(b) a pharmaceutically effective amount of an HDAI.

14. A combined preparation which comprises:

(a) one or more unit dosage forms of a death receptor ligand; and

(b) one or more unit dosage forms of a HDAI.